USDA

United States Department of Agriculture

Animal and Plant Health Inspection Service

Biotechnology Regulatory Services

4700 River Road
Riverdale, MD 20737

Dr. Robert L. Last
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Re: Confirmation of the regulatory status of gene-edited *Solanum lycopersicum* and *S. pennellii* lines for altered levels of metabolites.

Dear Dr. Last,

Thank you for your letter dated May 23, 2019, as amended on August 13, 2019, inquiring whether the tomato (*Solanum lycopersicum* and *Solanum pennellii*) lines described in your letter are regulated articles under 7 CFR part 340. Your letter describes tomato lines that have been gene-edited using the CRISPR/Cas9 system, resulting in altered levels of acylsugar metabolites.

The Plant Protection Act (PPA) of 2000 gives USDA the authority to oversee the detection, control, eradication, suppression, prevention, or retardation of the spread of plant pests or noxious weeds to protect the agriculture, environment, and economy of the United States.

USDA regulates the importation, interstate movement and environmental release (field testing) of certain genetically engineered (GE) organisms that are, or have the potential to be, plant pests. Regulations for GE organisms that are or have the potential to be plant pests, under the PPA, are codified at 7 CFR part 340, "Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which Are Plant Pests or Which There Is Reason To Believe Are Plant Pests." Under the provisions of these regulations, a GE organism is deemed a regulated article if it has been genetically engineered using a donor organism, recipient organism, or vector or vector agent that is listed in §340.2 and meets the definition of a plant pest, or that is an unclassified organism and/or an organism whose classification is unknown, or if the Administrator determines that the GE organism is a plant pest or has reason to believe it is a plant pest.

In your August 13, 2019 letter, you describe lines of *S. lycopersicum* and *S. pennellii* that contain insertions and/or deletions in target genes involved in acylsugar metabolism, rendering them nonfunctional. The CRISPR/Cas9 system was used to create these lines by *Agrobacterium*-mediated transformation of parental lines with a construct containing hCas9, small guide RNAs, and a selectable marker. Inserted sequences derived from plant pests include various regulatory elements and border regions from *Agrobacterium tumefaciens*, as well as regulatory elements from cauliflower mosaic virus and tobacco mosaic virus. Offspring with site-specific mutations and the corresponding phenotype of interest, but that do not contain any transgenes, were selected for further analysis. Absence of the 35S promoter and Cas9 sequence in offspring was confirmed by PCR.

Based on the information provided in your August 13, 2019 letter, USDA has concluded that your genome-edited tomato lines are not themselves plant pests. USDA has accepted your attestation that these genome-edited tomato lines contain only insertions and/or deletions produced as a result of the plant's DNA repair mechanism, and that all other inserted DNA was eliminated through breeding and selection. Therefore, consistent with previous responses to similar letters of inquiry, USDA would not consider your genome-edited tomato lines to be regulated pursuant to 7 CFR part 340. Additionally, neither *S. lycopersicum* nor *S. pennellii* is listed as a Federal noxious weed pursuant to 7 CFR part 360. USDA has no reason to believe that the altered metabolite phenotype in your tomato lines would increase the weediness of those plants.

Please be advised that the importation of wild and/or cultivated tomato seeds or plants, like all other tomato, will be subject to Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. For further information, should you plan to import these tomato seeds or plants, you may contact the PPQ general number for such inquiries at (877) 770-5990.

Please be advised that your described tomato lines, while not regulated by APHIS under 7 CFR part 340 may still be subject to other regulatory authorities such as FDA or EPA. To inquire about the regulatory status of your product with the EPA, please contact Alan Reynolds at 703-605-0515. To inquire about the regulatory status of your product with the FDA, please contact Robert Merker at 240-402-1226.

Should you become aware at any time of any issues that may affect the Agency's conclusion regarding this inquiry, you must immediately notify the Agency in writing of the nature of the issue. We hope that you appreciate our commitment to plant health and support for the responsible stewardship for the introduction of GE plants.

Sincerely,

Bernadette R. Juarez
APHIS Deputy Administrator
Biotechnology Regulatory Services
Animal and Plant Health Inspection Service
U.S. Department of Agriculture

2/14/2020
Date